

BIOGRAPHICAL SKETCH

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NAME: Fujikawa, Teppei

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Kyoto University, Kyoto, Japan	B.Sc.	03/2003	Agriculture
Kyoto University, Kyoto, Japan	Ph.D.	03/2008	Physiology
The University of Texas Southwestern Medical Center at Dallas	Postdoctoral	12/2013	Neuroscience and Neuroendocrinology

A. Personal Statement

My research interests center around the mechanism by which the central nervous system (CNS) regulates metabolic homeostasis, including glucose and lipid metabolism, as well as energy expenditure. Obesity and its associated diseases, such as diabetes have threatened the health and economic stability of both advanced and advancing countries. To understand the mechanism by which the CNS regulates metabolism and unravel a unique capability of the CNS to maintain metabolic homeostasis are key to pave the way for new therapeutic avenues for obesity and its related diseases. The past decade has seen huge strides in identifying the neuronal circuit and molecular mechanism by which the CNS regulates metabolism, but these studies are primarily investigated in metabolically stable conditions such as a sedentary setting. Animals have evolved in metabolically challenging environments, and the CNS likely plays a pivotal role in these environments as a coordinator of whole body metabolism. Thus, I believe that unveiling the mechanism by which the CNS regulates and maintains metabolism in metabolically challenging conditions is essential to understand the blueprint of regulation of metabolism, ultimately to develop novel treatments for obesity and metabolic diseases.

B. Positions and Honors

Position and Employment

2003-2005	Teaching Assistant, Division of Food Science and Biotechnology, Graduate school of Agriculture, Kyoto University, Kyoto, Japan
2005-008	Research Assistant, Division of Food Science and Biotechnology, Graduate school of Agriculture, Kyoto University, Kyoto, Japan
2008-2013	Postdoctoral fellow, Division of Hypothalamic Research, Department of Internal Medicine, The University of Texas Southwestern Medical Center
2014-2017	Instructor, Division of Hypothalamic Research, Department of Internal Medicine, The University of Texas Southwestern Medical Center
2017-	Assistant Professor, Department of Cellular and Integrative Physiology, The University of Texas

Other Experience and Professional Memberships

- 2011-2012 Committee Member (Japanese Representative), UT Southwestern, International Committee of Postdoctoral Association
- 2012-2014 Co-chair, UT Southwestern International Committee of Postdoctoral Association
- 2013-2016 Chair, Dallas Japanese Researchers Association

Honors

- 2011 Juvenile Diabetes Research Foundation Postdoctoral Fellowship
- 2013 Keystone Symposia (Diabetes — New Insights into Mechanism of Disease and its Treatment) Scholarship (Travel Award) for the poster presentation
- 2014 American Heart Association Scientist Development Grant (top 5% national)

C. Contributions to Science

1. Exercise increases a variety of neurotransmitters and molecules in the brain. However, these changes in the hypothalamus during exercise had not been determined. In my Ph.D. course at Kyoto University I investigated the role of transforming factor-beta, which is increased during exercise in the cerebrospinal fluid, in neuronal modulation of hypothalamic neurons and regulation of behavior. Additionally, I examined whether hypothalamic neurons are activated during exercise using microdialysis. I found that noradrenergic neurons projecting to the hypothalamus are activated during exercise, and later I found a particular neuronal population in the hypothalamus regulates fat metabolism during exercise.

- a. **Fujikawa, T.**, Matsumura, S., Yamada, H., Inoue, K., and Fushiki, T., Transforming growth factor-beta in the brain enhances fat oxidation via noradrenergic neurons in the ventromedial and paraventricular hypothalamic nucleus. *Brain Res*, (2007) 1173: p. 92-101.
- b. Kitaoka, R., **Fujikawa, T.**, Miyaki, T., Matsumura, S., Fushiki, T., and Inoue, K., Increased Noradrenergic Activity in the Ventromedial Hypothalamus during Treadmill Running in Rats. *J Nutr Sci Vitaminol (Tokyo)*, (2010) 56(3): p. 185-90.
- c. Miyaki, T., **Fujikawa, T.**, Kitaoka, R., Hirano, N., Matsumura, S., Fushiki, T., and Inoue, K., Noradrenergic projections to the ventromedial hypothalamus regulate fat metabolism during endurance exercise. *Neuroscience*, (2011) 190: p. 239-50.

2. Moving forward to the US as a postdoc, I started to investigate the mechanism underlying the leptin's anti-type 1 diabetic actions. The previous report demonstrated that leptin overexpression in whole body can reverse hyperglycemia in type 1 diabetes rodents model. I investigated the contributions of the brain to the leptin's anti-type 1 diabetic actions. A large body of literature have indicated the brain is critical site for the leptin's actions. However, this notion was not assessed regarding anti-type 1 diabetic actions. I found that the brain mediates the vast of majority of effects of leptin on type 1 diabetes. Further, I unraveled that GABAergic leptin-responsive neurons in the hypothalamus are key to the the leptin's anti-type 1 diabetic actions.

- a. **Fujikawa, T.**, Chuang, J.C., Sakata, I., Ramadori, G., and Coppari, R., Leptin therapy improves insulin-deficient type 1 diabetes by CNS-dependent mechanisms in mice. *Proc Natl Acad Sci U S A*, (2010) 107(40): p. 17391-6.
- b. **Fujikawa, T.**, Berglund, E.D., Patel, V.R., Ramadori, G., Vianna, C.R., Vong, L., Thorel, F., Chera, S., Herrera, P.L., Lowell, B.B., Elmquist, J.K., Baldi, P., and Coppari, R., Leptin engages a hypothalamic neurocircuitry to permit survival in the absence of insulin. *Cell metabolism*, (2013) 18: p.431-444

- c. **Fujikawa, T.** *, and Coppari, R. *, Living without insulin: the role of leptin signaling in the hypothalamus. *Front Neurosci*, (2015) 9, 108. *co-corresponding author

3. High physical activity or Exercise has metabolic benefit. To understand the mechanism underlying beneficial effects of exercise on metabolism is a foundation to design of new treatment for obesity and metabolic diseases. However the mechanism is still unclear, in particular, the contribution of the central nervous system was completely unknown. I investigated the role of steroidogenic factor-1 (SF-1), which is restrictedly expressed in the ventromedial hypothalamic nucleus (VMH) in the regulation of metabolism in the context of exercise. I found that mice lacking SF-1 in specifically in the VMH showed maladaptations to exercise training, such decreases skeletal muscle and increases fat mass compared to the control-exercise group. This suggest that the hypothalamus is key to metabolic adaptations to exercise.

- a. **Fujikawa, T.**, Castorena, C.M., Pearson, M., Kusminski, C.M., Ahmed, N., Battiprolu, P.K., Kim, K.W., Lee, S., Hill, J.A., Scherer, P.E., Holland, L.W., and Elmquist, K.J., SF-1 Expression in the Hypothalamus is Required for Beneficial Metabolic Effects of Exercise. *eLife*, (2016) Nov 22;5
- b. Choi, Y.H.*, **Fujikawa, T.* (co-first author)**, Lee, J., Reuter, A., and Kim, K.W., Revisiting the Ventral Medial Nucleus of the Hypothalamus: The Roles of SF-1 Neurons in Energy Homeostasis. *Front Neurosci*, (2013) 7: p. 71._

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/18YV7Fk7Ko6kl/bibliography/52069526/public/?sort=date&direction=ascending>.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

American Heart Association Scientist Development Grant 14SDG17950008 Fujikawa (PI)
01/01/2014-
12/31/2017

"A hypothalamic pathway mediates anti-type 1 diabetes actions of leptin"

The goal of this study is to identify the neuronal circuit in the hypothalamus which contributes to the anti-type 1 diabetes actions of leptin.

Role: PI

UT Health San Antonio Start-up Funding Fujikawa (PI)
02/01/2017-
01/30/2020

The Goal of this study is to unravel the mechanism by which the central nervous system regulates metabolism.

Role: PI

Completed Research Support

Juvenile Diabetes Research Foundation, Postdoctoral Fellowship 3-2011- 405 Fujikawa (PI)
09/01/2011-
08/31/2013

"Unraveling the brain neurons mediating the health-improving effects of leptin in type 1 diabetes"

The goal of this study is to identify the neuronal population in the brain which contributes to the mechanism by which leptin injection into the brain regulates glucose metabolism in type 1 diabetes model.

Role: PI

The Central Nervous System Regulates Whole Body Metabolism

Fujikawa Lab, Cellular and Integrative Physiology Department

Fujikawa lab is focusing on unraveling the mechanism by which the central nervous system (CNS) regulates whole body metabolic homeostasis such glucose and fat metabolism, energy expenditure, and food intake. Obesity and its associated diseases such diabetes have been increasing at the alarming rate and threatening our health and economy over the world. Understanding the mechanism underlying the regulation of metabolism is a fundamental step towards to designing new treatments for obesity and its associated diseases. The CNS, in particular the hypothalamus that is located in deep inside brain, is key to regulation of metabolism. However, the entire blue print of mechanism underlying CNS-regulation of metabolism is still unclear. Fujikawa lab has two major projects which the successful candidate in the Xiangya Medical School Research Program would spearhead.

Project 1: To determine the neuronal circuit that contributes to the regulation of glucose metabolism independently of insulin system

We previously demonstrated that the injection of leptin, which is derived from adipose tissue, into the brain can ameliorate hyperglycemia in insulin-deficient mice (Fujikawa et al., *PNAS*, 2010, PMID 20855609). We further showed that the hypothalamic neurons expressing leptin receptors are critical for this leptin's anti-diabetic actions (Fujikawa et al., *Cell Metabolism*, 2013, PMID 24011077). Using the comprehensive genetically-engineered mice, we will unravel the specific neurons which governs glucose metabolism without insulin.

Project 2: To determine roles of the CNS in metabolic adaptations to exercise

Exercise has beneficial effects on metabolism, for example, improvement of body composition (increases of skeletal muscle and decreases of fat depot). We previously showed that the hypothalamus is key to exercise-induced improvement of body composition (Fujikawa et al., *eLife*, 2016, PMID 27874828). We are currently tackling following two questions; 1) how exercise affects neuronal activity in the hypothalamus? 2) what the role of exercise-activated neurons in the hypothalamus? Using the state-of-art techniques, we will unravel the mechanism by which the CNS regulates metabolic adaptations to exercise.

During the program, the successful candidate can obtain following technique in Fujikawa Lab;

1. Molecular Technique; from basic and the state-of-art such from PCR, molecular cloning to CRISPR/Cas9 gene edit, and generate transgenic mice.
2. Neuroscience Technique; Optogenetics, chemogenetics, in vivo Ca^{2+} imaging, brain surgery for microinjection.
3. Decent Biochemical Technique: immunohistochemistry, in situ hybridization, Westernblotting, measure metabolites in the blood.
4. Transgenic Animal Handling; Maintain the transgenic mice (complex breeding and genotyping), collect blood and tissues.

Importantly, the successful candidate can gain a skill-set such logical and design thinking, writing a scientific article, presentation, and communication skill in English. She/he will have an opportunity to present her/his results in international conferences. Moreover, he/she will be expected to publish a paper as a first author in top-tier journals. Dr. Fujikawa recently joined to UT Health San Antonio, and he is truly motivated, energetic, and passionate about science. Join our team!